



Epidemiology of Sarcopenia in Community-Dwelling Older Adults

by

David Scott BHM (Hons)

Submitted in fulfilment of the requirements for the degree of Doctor of Philosophy

(Medical Research)

University of Tasmania, November 2010

Supervisors

Professor Graeme Jones

Associate Professor Leigh Blizzard

Doctor James Fell

Statement of Originality

This thesis contains no material which has been accepted for a degree or diploma by the University or any other institution, except by way of background information and duly acknowledged in the thesis, and to the best of my knowledge and belief no material previously published or written by another person except where due acknowledgement is made in the text of the thesis, nor does the thesis contain any material that infringes copyright.

(Signed)_____ (Date) _____

Statement of Authority of Access and Regarding Published Work

The publishers of the papers comprising Chapters 4, 5, 6, 7 and 9 hold the copyright for that content, and access to the material should be sought from the respective journals. The remaining non-published content of the thesis may be made available for loan and limited copying in accordance with the *Copyright Act 1968*.

(Signed)_____ (Date) _____

Statement of Co-Authorship

The following thesis includes work which has been submitted for publication in peer-reviewed journals. Publication details for each chapter are described in the “Publications arising from the thesis” section. Proportionate co-author contributions were as follows:

Chapters 4, 5, 8 & 9:

David Scott (60%), Leigh Blizzard (10%), James Fell (10%), Graeme Jones (20%).

Chapter 6:

David Scott (60%), Leigh Blizzard (10%), James Fell (10%), Graham Giles (5%),
Graeme Jones (15%).

Chapter 7:

David Scott (60%), Leigh Blizzard (10%), James Fell (10%), Changhai Ding (5%),
Tania Winzenberg (5%), Graeme Jones (10%).

(Signed)_____ (Date) _____

David Scott (Candidate)

(Signed)_____ (Date) _____

Graeme Jones (Primary Co-supervisor)

Statement of Ethical Conduct

The research associated with this thesis abides by the international and Australian codes on human and animal experimentation, the guidelines by the Australian Government's Office of the Gene Technology Regulator and the rulings of the Safety, Ethics and Institutional Biosafety Committees of the University.

(Signed)_____ (Date) _____

Abstract

Background

Older adult functional declines may be partly attributable to sarcopenia (the age-related loss of skeletal muscle mass and function), and also age-related fat gains. The associations of lifestyle factors with skeletal muscle and body fat changes are unclear.

Aim

To investigate how measures of ambulatory activity, dietary nutrient intake, vitamin D, chronic disease and medication use, associate with changes in muscle mass, lower-limb function, falls risk and body fat in community-dwelling older adults.

Materials and Methods

Total N = 875 adults aged 50 - 80 years (51% female; mean age = 62 ± 7 years) participated at baseline and 2.6 ± 0.4 years later. Appendicular lean mass (ALM), leg lean mass, and body fat were assessed by Dual-energy X-ray Absorptiometry (DXA). Lower-limb muscle function was assessed by dynamometry, and leg and whole body muscle quality (LMQ and WBMQ) was calculated. Falls risk score was assessed by a Physiological Profile Assessment (PPA). Study factors including ambulatory activity (AA) measured by pedometer, 25-hydroxyvitamin D (25OHD) by radioimmunoassay, radiographic osteoarthritis (ROA) by X-ray, and dietary nutrient intake, pain, and statin medication use reported by questionnaire, were assessed.

Results

Total body and trunk fat mass were negatively associated with seasonally-adjusted pedometer-determined AA in both men and women in cross-sectional analyses, but men only

in prospective analyses. In women only, significant positive associations for leg strength and LMQ, and also WBMQ, with AA were observed. Energy-adjusted protein, iron, magnesium, phosphorus, and zinc intakes were significant positive predictors of change in ALM, while retinol was a negative predictor of change in ALM. Nutrient intakes did not predict changes in knee extension strength. 25OHD positively predicted change in leg strength and LMQ, and change in 25OHD was also predicted by baseline percentage ALM (%ALM), leg strength, LMQ and AA, after adjustment for sun exposure and body fat. Knee and hip pain measures predicted deleterious changes in muscle function and falls risk in women only; no muscle function associations were observed for ROA in either sex. Over time, statin users demonstrated decreased leg strength and LMQ, and increased falls risk, compared to non-users.

Conclusions

This series of related analyses of a prospective population-based study of community-dwelling older adults provides considerable insight into the epidemiology of sarcopenia. Interventions focused on maintaining or improving behaviours including physical activity, diet, and sun exposure, as well as more effective management of chronic disease, may be efficacious in the prevention of skeletal muscle mass loss, functional decline, and obesity.

Acknowledgements

The Tasmanian Older Adult Cohort Study (TASOAC) was supported by the National Health and Medical Research Council of Australia, Arthritis Foundation of Australia, Tasmanian Community Fund, and the University of Tasmania Institutional Research Grants Scheme. I would also like to acknowledge the University of Tasmania and Menzies Research Institute, who co-funded my Tasmanian Graduate Research Scholarship. Many thanks to the TASOAC participants who generously gave of their time to make this research possible, and to the TASOAC staff and volunteers who worked tirelessly on the project, in particular Catrina Boon and Dale Pitt. I am also grateful to the administrative staff of the Menzies Research Institute for their assistance throughout my PhD candidature.

I would like to thank past and present PhD students for their support and friendship, with a special mention to Dawn Dore, Kara Martin, Stella Foley, Michelle Callisaya, Kylie Smith, and Laura Laslett. Thank you also to the many academic staff at the Menzies who are not part of my supervisory team, but have always been willing to provide much needed advice. These include Doctors Changhai Ding and Tania Winzenberg, who were co-authors in our vitamin D analysis.

I am extremely fortunate to have had the opportunity to work under a primary supervisor of the distinction of Professor Graeme Jones, and his great passion and excitement for research has certainly rubbed off on me. Graeme continually sets high standards for his students and I know that the skills I have learnt under his tutelage will be of huge benefit throughout my research career. My understanding of statistics has developed significantly under my co-supervisor Associate Professor Leigh Blizzard, and I'm very grateful for his continued patience and guidance. Co-supervisor Doctor James Fell has provided expert advice, and has also been a wonderful mentor and friend, since providing me with the opportunity to complete my Honours in 2006.

Finally, I would like to sincerely thank my parents Stephen and Judy, and my partner Rachel, who have been continual sources of emotional (and financial) support throughout my many years as a student. Their belief in me has allowed me the opportunity to follow my passion, and I hope the work within this thesis justifies in some small way the significant sacrifices they have made on my behalf.

Publications Arising from the Thesis

Chapter 4: Scott D, Blizzard L, Fell J, & Jones G. Ambulatory activity, body composition and lower-limb muscle strength in older adults. *Medicine and Science in Sports and Exercise* (2009) 41: 383-9.

Chapter 5: Scott D, Blizzard L, Fell J, & Jones G. Prospective associations between ambulatory activity, body composition and muscle function in older adults. *Scandinavian Journal of Medicine and Science in Sports* (available on-line 28/08/2010) DOI: 10.1111/j.1600-0838.2010.01229.x.

Chapter 6: Scott D, Blizzard L, Fell J, Giles G, & Jones G. Associations between dietary nutrient intake, muscle mass and strength in community-dwelling older adults: The Tasmanian Older Adult Cohort Study. *Journal of the American Geriatrics Society* (accepted for publication 02/07/2010).

Chapter 7: Scott D, Blizzard L, Fell J, Ding C, Winzenberg T, & Jones G. A prospective study of the associations between 25-hydroxyvitamin D, sarcopenia progression, and physical activity in older adults. *Clinical Endocrinology* (2010) 73: 581-7.

Chapter 8: Scott D, Blizzard L, Fell J, & Jones G. A prospective study of the associations between self-reported pain, radiographic osteoarthritis and sarcopenia in community-dwelling older adults. *Pain* (manuscript under preparation).

Chapter 9: Scott D, Blizzard L, Fell J, & Jones G. Statin therapy, muscle function and falls risk in community-dwelling older adults. *Quarterly Journal of Medicine* (2009) 102: 625-33.

Scientific Presentations Arising from the Thesis

- 2009** 19th International Association of Gerontology and Geriatrics World Congress
(Paris, France).
–Ambulatory activity, nutrient intake and statin use as determinants of sarcopenia in community-dwelling older adults” (Oral presentation).
- 2009** 8th National Emerging Researchers in Ageing Conference
(Melbourne, Australia).
–The Recommended Dietary Intake (RDI) for protein and indicators of sarcopenia in community-dwelling older adults” (Poster presentation).
- 2008** 3rd Australian Association for Exercise and Sport Science Conference
(Melbourne, Australia).
–Cross-sectional associations between leg strength, body composition and pedometer-determined ambulatory activity in older adults” (Oral presentation).

Table of Contents

Statement of Originality.....	II
Statement of Authority of Access and Regarding Published Work	III
Statement of Co-Authorship	IV
Statement of Ethical Conduct.....	V
Abstract	VI
Acknowledgements.....	VIII
Publications Arising from the Thesis	X
Scientific Presentations Arising from the Thesis	XI
List of Abbreviations.....	XII
List of Tables	XV
List of Figures.....	XVII
Table of Contents	XIX
Synopsis	1
Chapter 1 - Epidemiology of Sarcopenia in Older Adults	7
1.1 Population ageing.....	8
1.2 Defining sarcopenia	10
1.2.1 History and controversy.....	10
1.2.2 Rate of age-related skeletal muscle mass and function decline	11
1.2.3 Disassociation between skeletal muscle mass and function changes	13
1.3 Prevalence of sarcopenia	15
1.4 Etiology of sarcopenia.....	19
1.4.1 Prelude	19
1.4.2 Genetics and development.....	19
1.4.3 Age-related body composition changes	21
1.4.4 Systemic low-level inflammation and endocrine dysfunction.....	26
1.4.5 Physical activity.....	31
1.4.6 Diet and metabolism	35
1.4.7 Vitamin D	40
1.4.8 Chronic disease	45
1.4.9 Medication use.....	49
1.4.10 Summary of the potential etiology of sarcopenia	53
1.5 Outcomes of sarcopenia	57

1.6	Treatment strategies for sarcopenia	61
1.6.1	<i>Physical activity interventions</i>	61
1.6.2	<i>Nutritional supplementation</i>	63
1.6.3	<i>Hormonal supplementation</i>	65
1.7	Summary	68
Chapter 2 - Research Questions		70
Chapter 3 - Methodology		72
3.1	Prelude	73
3.2	Study population and design	73
3.3	Outcome measures	75
3.3.1	<i>Body composition</i>	75
3.3.2	<i>Knee extension strength</i>	76
3.3.3	<i>Leg strength and muscle quality</i>	77
3.3.4	<i>Falls risk</i>	79
3.4	Study factors.....	81
3.5	Covariates.....	81
3.5.1	<i>General questionnaire</i>	81
3.5.2	<i>Anthropometrics</i>	84
3.6	Sample size and role of the candidate in the TASOAC study.....	84
3.7	Statistical analyses	85
3.8	Ethical considerations	85
Chapter 4 - Cross-sectional Associations of Ambulatory Activity, Body Composition and Muscle Function.....		86
4.1	Introduction	87
4.2	Materials and methods	89
4.2.1	<i>Measurement of ambulatory activity</i>	89
4.2.2	<i>Statistical analysis</i>	90
4.3	Results.....	92
4.4	Discussion	97
Chapter 5 - Prospective Associations of Ambulatory Activity, Body Composition and Muscle Function.....		103
5.1	Introduction	104
5.2	Materials and Methods.....	106
5.2.1	<i>Measurement of ambulatory activity</i>	106

5.2.2 Statistical analysis.....	107
5.3 Results	109
5.4 Discussion	114
Chapter 6 - Prospective Associations of Dietary Nutrient Intake, Muscle Mass and Muscle Function	119
6.1 Introduction	120
6.2 Materials and Methods.....	122
6.2.1 Assessment of dietary nutrient intake.....	122
6.2.2 Statistical analysis.....	122
6.3 Results	124
6.4 Discussion	129
Chapter 7 - Prospective Associations of 25-Hydroxyvitamin D, Muscle Mass, Muscle Function and Ambulatory Activity.....	133
7.1 Introduction	134
7.2 Materials and Methods.....	136
7.2.1 Measurement of 25-hydroxvitamin D, sun exposure, and supplement use	136
7.2.2 Statistical analysis.....	136
7.3 Results	139
7.4 Discussion	144
Chapter 8 - Prospective Associations of Pain, Radiographic Osteoarthritis, Muscle Mass, Muscle Function and Falls Risk	148
8.1 Introduction	149
8.2 Materials and Methods.....	151
8.2.1 Pain assessment	151
8.2.2 Radiographic osteoarthritis assessment.....	151
8.2.3 Statistical analysis.....	152
8.3 Results	154
8.4 Discussion	159
Chapter 9 - Prospective Associations of Statin Use, Muscle Mass, Muscle Function and Falls Risk	164
9.1 Introduction	165
9.2 Materials and methods	167
9.2.1 Assessment of statin use.....	167
9.2.2 Statistical analysis.....	167

9.3 Results	169
9.4 Discussion	174
Chapter 10 - Summary and Future Directions	180
10.1 Summary	181
10.2 Future Directions	186
Bibliography	192
Appendices	240